PATENT
Docket No. 388512010900

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Patent Application of:	Confirmation No.: 6212
Lawrence M. KAUVAR et al.	Examiner: David J. Venci
Application No.: 10/681,013	Group Art Unit: 1641
Filed: October 7, 2003	
For: METHODS TO DETERMINE NUMBERS OF PARTICLES IN MULTIPLEXED ASSAYS (AS AMENDED)	

REPLY BRIEF

MS Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This brief replies to the Examiner's Answer mailed 6 August 2007. A Request for Oral Hearing is enclosed.

Preliminary Formal Matter

The Examiner objected to the inclusion of the term "hue" in the summary of the invention, apparently because this word is not used in the claim. Applicants are unaware that there is any prohibition of using a word not contained in the claim to describe the invention. As is clear from the specification, the word "hue" is used to describe the collection of wavelengths that comprise the characterizing signal set forth in subparagraph (a) of claim 1. See page 2, beginning third line from the bottom. Applicants also fail to see the relevance of this comment to the merits.

Substantive Matters

First, claims 3-4 (and therefore, effectively 5-6 dependent thereon) were requested to be considered separately. These claims are directed to a method for determining the distribution of multiple target substances wherein the number of labels at a location in the sample is assessed by measuring the intensity of the signal emitted from the second signal generating moiety directly attached to the particulate supports.

Respectfully, applicants believe the Examiner is incorrect in interpreting paragraph 69 of Nie (US 2003/0148544) as describing this method. The quoted section of paragraph 69: "The intensity of the signal generated by the tag attached to the *target* molecule will be in direct proportion to the amount of target present in the sample" clearly refers to the entity marked "F" in figure 5 which is attached to the *target* as required by paragraph 69 not to the particulate support. The "tag" does not refer to the green quantum dot with the marking / which is what the Examiner asserts corresponds to the second signal generating moiety of subparagraph (b) in claim 1. Therefore, claims that require assessing the number of labels by measuring the intensity of the signal from the second signal generating moiety are not anticipated.

As applicants have pointed out previously, it is mere accident that the level of the green (/) quantum dot is present at the same level in all of the particles in figure 5 of Nie and this is only possible because only three different particulate labels are depicted. In order to distinguish a fourth particulate label with only forward slash (/), backward slash (\) and crosshatch (x), the level of the green quantum dot would need to be varied.[*]

Thus, it is apparent that Nie does not teach using the second signal generating moiety consisting of a single fluorophore directly attached to said particulate support as a measure of the number of labels at a particular location. Instead, Nie uses a fluorescent tag attached to the target itself, not to the particulate support.

With respect to claims 1, 2 and 7, the Examiner asserts that the composition is expressly taught by Nie and that therefore case law directed to inherent anticipation does not apply. Respectfully, applicants believe this is in error. What is expressly taught by Nie is that there is a *characterizing* signal comprised of three different types of quantum dots, one of which happens to be present at a constant amount in all three types of particulates. There is no express statement that this green quantum dot is a separate signal generating moiety that is not part of the first characterizing signal as set forth in subparagraph (b).

As noted in the Brief on Appeal, the disclosure of an assertedly anticipating reference that does not expressly anticipate (as Nie does not) must inevitably yield the result that falls within the scope of the claim. This would not be true of Nie, because Nie does not recognize that a separate second signal generating moiety apart from the characterizing moiety is required. It is only the particular array selected with a minimal number of particulate labels that permits the result that one of the quantum dots need not vary. The artisan following the directions of Nie would clearly not construct, each and every time, a series of particulates wherein one of the quantum dots is held constant in all of the members of the composition because Nie provides no instructions to do so.

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[*] It should be noted that figure 5 of Nie has an obvious error in that probe No. 1 and probe No. 2 are identical; the second depiction down in this figure is simply the first depiction bound to target. Thus, the second, third and fourth particulates in figure 5 should be labeled, respectfully, probe No. 1, probe No. 2 and probe No. 3.

Although the rejection is based on anticipation rather than obviousness, applicants point out that Nie teaches away from the invention because Nie relies on a fluorescent label attached to the target rather than to the particles themselves as an index of amount.

With respect to the rejection of claims 5 and 6 over the combination of Nie with Kauvar (US 2001/0044116), perhaps applicants' arguments have been misunderstood. Kauvar does teach the use of multihued beads in a particular context as required by these claims; however, there is no suggestion in Kauvar that there is any need to determine concentrations in this context, and thus there would be no need to utilize the method of the invention for this purpose. More importantly, since the method of Nie is not the method of the invention, the combination of Nie with Kauvar does not lead to the invention as claimed.

Summary

The anticipation argument made by the Examiner with regard to claims 3-4 (and 5-6) requires a slight-of-hand whereby the *tag* associated with the *target* described in paragraph 69 of Nie is replaced by the second signal generating moiety identified (only by the Examiner, not by Nie) as the green quantum dot in figure 5. Even if the green quantum dot of figure 5 is interpreted as the second signal generating moiety of paragraph (b) of claim 1, paragraph 69 of Nie does not describe using this to determine the number of labels.

With respect to claims 1, 2 and 7, Nie fails to expressly teach that the green quantum dot of figure 5 is a second signal generating moiety apart from the characterizing moiety on the particles. Instead, Nie expressly describes the assembly of crosshatched dots in this illustration as the characterizing moiety. Any inherent anticipation is based on a simple accidental coincidence that because so few particles are illustrated, additional variation in the numbers of quantum dots is not required in order to make the particles distinguishable. Following the directions of Nie, one would not inevitably generate particulates with a second signal generating moiety distinct from the characterizing one.

For these reasons, applicants believe claims 1-7 are in position for allowance and reversal of the rejection and passage of the claims to issue is respectfully requested.

The Assistant Commissioner is hereby authorized to charge any additional fees under 37 C.F.R. § 1.17 that may be required by this Brief, or to credit any overpayment, to **Deposit Account No. 03-1952**.

Respectfully submitted,

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